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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/713,177	11/15/2000	Glen H. Erikson	E1047/20048	3217

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EXAMINER	
CHUNDURU, SURYAPRABHA	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 03/11/2003

23

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/713,177	ERIKSON ET AL.	
	Examin r	Art Unit	
	Suryaprabha Chunduru	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-63* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Acknowledgement is made for the request to establish continued prosecution application (RCE) (Paper NO. 22) filed on February 6, 2003. The request for RCE is accepted and is established with the status of the application as follows:

a. the filling date of this RCE is established as 11/15/2000;

b. Claims 1-63 are pending.

2. Applicants' response to the earlier office action (Paper No. 21) filed on 2/6/03 is considered and has been entered.

Response to Arguments

3. Applicant's response to the office action (Paper No.21) is fully considered and found persuasive in view of arguments and IDS submitted.

4. With reference to the rejection maintained in the previous office action under 35 U.S.C. 112, first paragraph, applicants' arguments and IDS have been fully considered and the rejection is moot in view of the arguments and enablement of Watson-Crick base pairing involving more than two strands of DNA as shown in IDS.

New Grounds of Rejection

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

A. Claims 1-6, 13, 24-29, 34, 36, 62-63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eckhart et al. (J Biol Chem., Vol.274, No.5, pp. 2613-2615, 1999) in view of Deng et al. (Biopolymers, Vol. 35, No. 6, pp. 677-681, 1995).

Eckhart et al. teach a catalytic composition comprising a probe containing nucleobase sequence and one scissile linkage sequence, an enzyme adapted to cleave said at least one scissile linkage sequence, a target nucleic acid containing at least one target nucleobase sequence associated by complementary base pairing to form a multiplex structure and a hybridization medium containing said probe, said enzyme and said target nucleic acid wherein the target-probe complex base pairing comprises complementary base pairing (see page 2613, column 1, paragraph 1, column 2, paragraph 4). Eckhart et al. also teach a method for assaying binding comprising, providing said probe containing a scissile linkage, an enzyme that cleaves the said scissile linkage and a target nucleic acid, combining said probe, enzyme and the target in a hybridization medium containing water and buffer and one promoter, incubating said hybridization medium to form a target-probe hybrid multiplex structure by complementary base pairing (see page 2613, column 2, paragraphs 3-4); detecting the alternatively spliced (unbound

probe fragments) to assay binding between said probe and said target. (see page 2614 column 1, paragraph 2). Eckhart et al. also teach (i) single-stranded probe and a double stranded target (see page 2613, column 2, paragraphs 2-4); (ii) the method includes incubation temperature at 37 C and pH of hybridization medium about 5 (see page 2613, column 2, paragraphs 2-4); (iii) comprises intercalating fluorophore agent as ethidium bromide (see page 2613, column 2, paragraphs 2-4); (iv) Na^+ cation concentration of 50mM and incubation time not more than 24 hours (see page 2613, column 2, paragraphs 2-4) Although Eckhart et al. teach complementary base pairing Eckhart et al. did not teach Watson-Crick bonding between probe and target nucleobase sequences.

Deng et al. teach a multiplex structure comprising a first and second strand containing sequence of nucleobases, wherein first and second strand are associated with each other by Watson-Crick base pairing (see page 680, column 1, Fig.3, paragraph 3, page 681, column 1, paragraph 1); a third and fourth strand containing sequence of nucleobases, wherein fourth strand sequence is associated with said second strand by Watson-Crick base pairing, and third and fourth strands are associated by Watson-Crick base paring (see page 680, column 1, Fig. 3, paragraph 3, page 681, column 1, paragraph 1). Deng et al. further disclose that the multiplex structure was a synthetic quadruplex (oligonucleotides) made up of nucleic acid comprising DNA (see page 678, column 1, paragraphs 1-2). Each nucleic acid strand in the multiplex structure were complementary to each other, that is antiparallel to each other and each nucleobase binds to more than two other nucleobases and substantially free of Hoogsteen bonding (see page 680, column 1, Fig. 3, paragraph 3). Each strand in the multiplex comprises at least 8-12 base pairs (see page 680, column 2, paragraph 1, page 681, column 1, paragraph 1);

multiplex structure is free of a solid support and non electrically conductive or bound to a solid support which is electrically conductive (electrophoresis gel) (see page 680, column 1, Fig.3, paragraph 3, column 2, Fig.4, paragraph 1). However, Deng et al. did not teach nucleic acid strands comprising RNA, mina or genomic DNA, and multiplex structure substantially free of G-G quartets and content of urine and pyramiding bases of the nucleic acid sequences.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the method and composition of DNA hierodule complex as taught by Elkhart et al. with the Watson-Crick base paring forming parameters as taught by Deng et al. which facilitate Watson-Crick base pairing nucleic acid strands in a multiplex structure because Deng et al. states that "potassium can effectively induce stability in quadruple structure and transition from duplex to quadruple structures is clearly salt and sequence dependent" (see page 680, column 1, paragraph 3, column 2, paragraph 1). An ordinary practitioner would have been motivated to combine the teachings as taught by Eckhart et al. with the parameters or reaction conditions as taught by Deng et al. in order to achieve the expected advantage of developing a more stable structure because the inclusion of the parameters as taught by Deng et al. would facilitate Watson-Crick base pairing and enhance the stability of the binding.

B. Claims 1-63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eckhart et. al. (J Biol Chem., Vol.274, No.5, pp. 2613-2615, 1999) in view of Erikson et al. (USPN. 6,420,115).

Eckhart et al. teach a catalytic composition comprising a probe containing nucleobase sequence and one scissile linkage sequence, an enzyme adapted to cleave said at least one scissile linkage sequence, a target nucleic acid containing at least one target nucleobase sequence

associated by complementary base pairing to form a multiplex structure and a hybridization medium containing said probe, said enzyme and said target nucleic acid wherein the target-probe complex base pairing comprises complementary base pairing (see page 2613, column 1, paragraph 1, column 2, paragraph 4). Eckhart et al. also teach a method for assaying binding comprising, providing said probe containing a scissile linkage, an enzyme that cleaves the said scissile linkage and a target nucleic acid, combining said probe, enzyme and the target in a hybridization medium containing water and buffer and one promoter, incubating said hybridization medium to form a target-probe hybrid multiplex structure by complementary base pairing (see page 2613, column 2, paragraphs 3-4); detecting the alternatively spliced (unbound probe fragments) to assay binding between said probe and said target. (see page 2614 column 1, paragraph 2). Eckhart et al. also teach (i) single-stranded probe and a double stranded target (see page 2613, column 2, paragraphs 2-4); (ii) the method includes incubation temperature at 37 C and pH of hybridization medium about 5 (see page 2613, column 2, paragraphs 2-4); (iii) comprises intercalating fluorophore agent as ethidium bromide (see page 2613, column 2, paragraphs 2-4); (iv) Na^+ cation concentration of 50mM and incubation time not more than 24 hours (see page 2613, column 2, paragraphs 2-4) Although Eckhart et al. teach complementary base pairing Eckhart et al. did not teach Watson-Crick bonding between probe and target nucleobase sequences.

Erikson et al. teach a multiplex structure comprising (i) RNA, genomic DNA sequences (see column 4, lines 58-66); (ii) multiplex formation with major and minor grove binding proteins which facilitate appropriate placement of nucleic acid strands in major groove (see column 6, lines 57-67); (iii) multiplex with substantially free of G-G quartets (do not require the

presence of homopurine or homopyrimidine sequences) (see column 3, lines 1-10); (iv) nucleic acid strands of multiplex comprise 5 to 50 base pairs long and 8 x $3.3x10^9$ base pairs long nucleic acid strands (see column 3, lines 13-15); (v) nucleic acid sequences contain 25% to 75% purine bases and 75% to 25% pyrimidine bases in any order (see column 3, lines 10-12); and (vi) nucleic acid strands could be obtained by PCR amplification (see column 6, lines 19-20); Concentration of probe or target sequence not more than $5x\ 10^{-10}$ M (see column 21, lines 33-39).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the method of hybridization assay as taught by Eckhart et al. with the multiplex forming parameters as taught by Erikson et al. which facilitate Watson-Crick base pairing nucleic acid strands in a multiplex structure because Erikson et al. states that "specific binding between complementary bases occurs under a wide variety of conditions having variations in temperature, salt concentration, electrostatic strength and buffer composition. Unlike many Hoogsteen-type multiplexes, which are unstable, the Watson-Crick multiplexes are stable over a wide range of conditions, and does not require longer reaction times" (see column 6, lines 40-56). An ordinary practitioner would have been motivated to combine the method of hybridization assay as taught by Eckhart et al. with the parameters or reaction conditions as taught by Erickson et al. in order to achieve the expected advantage of developing a more stable structure because the inclusion of the parameters as taught by Erikson et al. would facilitate Watson-Crick base pairing and enhance the stability of the binding in the hybridization assay.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 703-305-1004. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Suryaprabha Chunduru
March 7, 2003

JEFFREY FREDMAN
PRIMARY EXAMINER